ARGUMENT

(1) Claims 5-7 and 9 stand rejected under 35 U.S.C. § 103 as being unpatentable over Huth et al. (WO 00/27819), Patani et al. (Chem. Rev. 1996, 3147-3176), Fotouhi et al. (US 2002/0052512 and In re Wood (199 USPQ 137). Appellants assert that the Examiner has failed to establish a prima facie case of obviousness.

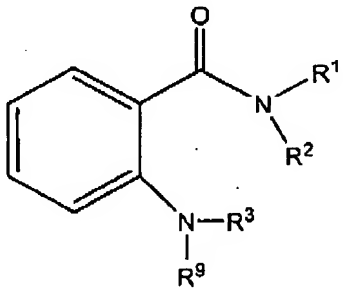
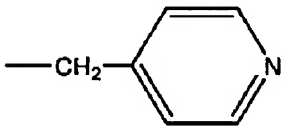
(2) Claim 31 stands rejected under 35 U.S.C. § 103 as being unpatentable over Huth et al. (WO 00/27819) in view of Patani et al. (Chem. Rev. 1996, 3147-3176), Fotouhi et al. (US 2002/0052512 and In re Wood (199 USPQ 137). Appellants assert that the Examiner has failed to establish a prima facie case of obviousness.

(3) Claims 30 and 34 stand rejected under 35 U.S.C. § 103 as being unpatentable over Huth et al. (WO 00/27819) in view of Patani et al. (Chem. Rev. 1996, 3147-3176) and In re Wood (199 USPQ 137). Appellants assert that the Examiner has failed to establish a prima facie case of obviousness.

I. The Examiner Has Failed To Establish A Prima Facie Case Of Obviousness In Relation To Claims 5-7 and 9

The Examiner has rejected claims 5-7 and 9 under 35 U.S.C. § 103 as being unpatentable over Huth et al. (WO 00/27819), Patani et al. (Chem. Rev. 1996, 3147-3176), Fotouhi et al. (US 2002/0052512 and In re Wood (199 USPQ 137).

Appellants assert that the Examiner has failed to establish a prima facie case of obviousness.

The Examiner provides an explanation of the basis for the rejection within the Final Office Action at page 5 line 7, to page 7 line 12. Specifically, in attempting to support the rejection the Examiner notes that examples 2.39 and 2.56 of Huth et al. disclose compounds of the formula  where R^2 and R^9 are hydrogen, R^3 is  , and R^1 is indol-5-yl, or 4-chloropyridyl. Then the Examiner asserts that:

> "Patani et al. teach ring replacements of NH for CH_2 in aromatic and aliphatic rings. See pages 3158-3159. This would make the 5-yl and 6-yl indoles, as well as quinoline/isoquinoline, equivalent structures."

(Final Office Action at page 6 lines 12-14). The Examiner then proceeds to assert that:

> "Fotouhi et al. teach that substituting and [sic] 2,3-dihydro-1H-indole for indole give [sic] molecules with the same utility and comparable activities. See Example 315 on page 109, Example 38 on page 110, and the activities on page 136, column 2."

(Final Office Action at page 6 lines 15-17). The Examiner then notes that hydrogen and methyl would be considered obvious variants under the holding of In re Wood.

Appellants assert that in comparing the prior art against the claimed invention the Examiner interprets the teachings of both Patani and Fotouhi far more broadly than is appropriate. To assert, as done here by the Examiner, that Patani broadly teaches that

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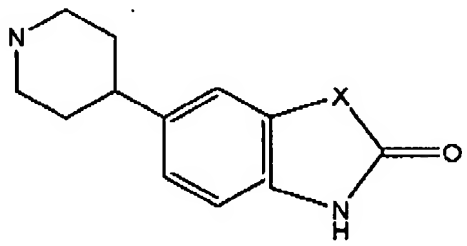
* Appellants question the inclusion of judicial decisions, such as In re Wood, as prior art references. While the holdings of judicial precedent can certainly be relied upon to support the underlying rationale of a rejection, the

any and all "replacements of NH for CH_2 in aromatic and aliphatic rings"† will ***always*** provide "equivalent" structures, with "equivilant" properties relative to ***any and all*** biologic targets, finds absolutely no support within a fair reading of the reference. Indeed a person of skill in the art would recognize such attempts to draw broad over-arching trends across diverse scaffolds and biologic targets, as a gross oversimplificaiton.

The Examiner's ultimate conclusion that Patani et all establish the equivalency of all 5-yl and 6-yl Indoles under all circumstances is not even supported by the cited text of the reference (i..e., page 3158-3159). A review of the actually cited pages reveals a disclosure of 2 separate chemical scaffods that both employ certain **5-yl** indolinone-type fragements (see e.g., Figure 34 (compound 52), and Figure 36). Each of these compound is distinct in both structure and chemical activity.

The first cited scaffold in Patani (Figure 34, compound 52) discloses a genus of **PDE III modulators** of the following formula::



X = CH_2, NH

This genus covers both

(1) **piperadin-5-yl**, 2,3-dihydro benzimidazol**ones**; and

(2) **piperadin-5-yl**, indoline **-2-one**

The cited scaffold thus encompasses only **5-yl** substitied 2,3-dihydrobenzimidazol**ones**/ or indolin**ones**

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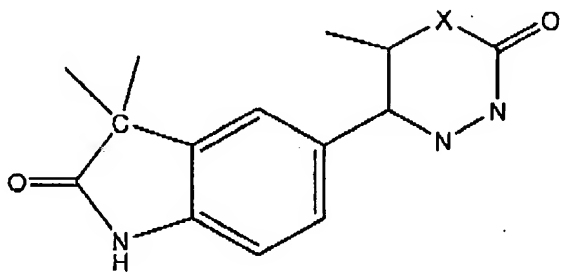
judicial decision itself does not appear to be properly categorized as "prior art".

The second cited scaffold in Patani (Figure 36, compound 54) disclose a genus of **Cardiotonic agents** of the following formula:



Like the previously cited scaffold, this second scaffold also encompasses only **5-yl** substitied 2,3-dihydrobenzimidazol**ones**/ or indolin**ones**

As is readily apparent, there are a number of significant logical gaps between this cited disclosure and the extremely broad interpretation afforded by the Examiner:

- In making the broad conclusion the Examiner apparently sees fit to discount any activity effects that might be attributable to the differing specific substituents at the 5 position of the cited scaffolds in Patani.
- The cited compounds are all 5-yl substituted indolin**one** compounds. The Examiner does not provide any rational for the implicit equation of indoles and indolinones.
- Contrary to the Examiner's position, the cited reference does not disclose any purported equivalency between either 5-yl or 6-yl indoles. Indeed, the reverence only discloses 5-yl substituted indolinones. How the Examiner now draws a conclusion as to the universal equivilancy of any and all corresponding 6-yl isomers, is beyond Appellants comprehension.
- The Examiner does not explain how Patani's discosure of certain PDE III modulators in Figure 34, and other structurally distinct

† Appellants note this NH could not be substituted with CH_2 in aromatic systems without violating rules of

> Cardiotonic agents in Figure 36, would lead any person of skill in the art to reasonably expect that certain fragments of the scaffold could prove useful in the seach for kinase inhibitors, such as inhibitors of VEGF/KDR.

Morever, the Examiner has not explained how a person of skill in the art, reviewing Fotouhi's disclosure (which relates to ICAM inhibitors of a stucturally distinct scaffod), would conclude that the substitution of 2,3, dihydro-1-H indole for indole -- on the completely different kinase inhibitor scaffold covered by the claims on appeal – would be expected to yeild compounds of similar propreties.The Advisory Action indicates that this rejection has been maintained because:

> "Applicant has not provided evidence of the biosteric changes not working, and the base compounds being modified by the 103(a) rejection are of similar structure and have the same utility" (See Form PTO-303 Continuation Sheet).

First: Appellants stress that the Examienr has improperly placed a burden on them to rebut a case that has not been proprely supported in the first instance. Until the Examienr presents a properly supported prima facie case of unpatentabiliy under section 103, there is no need for an applicant to present evidence to rebut the Examiner. **Seond:** The Examiner incorrectly asserts that the cited prior art compounds are of similar structure and have the same utility. All of these compounds are designed to affect different targets that VEGF/KDR (e.g., PDE III modulators, Cardiotonic agents and ICAM inhibitors).

II. The Examiner Has Failed To Establish A Prima Facie Case Of Obviousness In Relation To Claim 31

The Examiner has rejected claim 31 under 35 U.S.C. § 103 as being unpatentable over Huth et al. (WO 00/27819) in view of Patani et al. (Chem. Rev. 1996, 3147-3176), Fotouhi et al. (US 2002/0052512 and In re Wood (199 USPQ 137).

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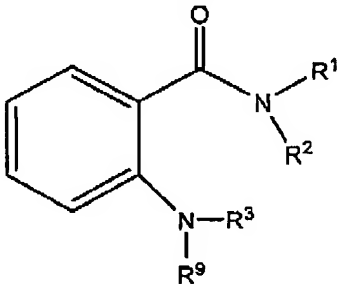
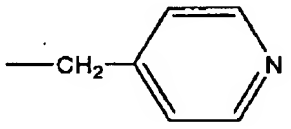
Appellants assert that the Examiner has failed to establish a prima facie case of obviousness.

The Examiner provides an explanation of the basis for the rejection within the Final Office Action at page 10 line 3, to page 11 line 12. Specifically, in attempting to support the rejection the Examiner notes that example 2.56 of Huth et al. discloses a compound of the formula  where R^2 and R^9 are hydrogen, R^3 is  , and R^1 is indol-5-yl. Then the Examiner asserts that:

> "Patani et al. teach ring replacements of NH for CH_2 in aromatic and aliphatic rings. See pages 3158-3159. This would make the 5-yl and 6-yl indoles equivalent structures."

(Final Office Action at page 10 lines 17-19). The Examiner then proceeds to assert that:

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(Final Office Action at page 11 lines 1-3). The Examiner then notes that hydrogen and methyl would be considered obvious variants under the holding of In re Wood.

Appellants assert that in comparing the prior art against the claimed invention the Examiner interprets the teachings of both Patani and Fotouhi far more broadly than is appropriate. To assert, as done here by the Examiner, that Patani broadly teaches that ***any*** and all "replacements of NH for CH_2 in aromatic and aliphatic rings" will ***always*** provide "equivalent" structures, with "equivilant" properties relative to ***any and all***

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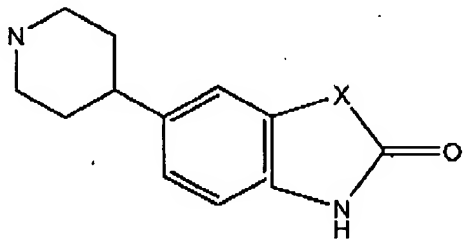

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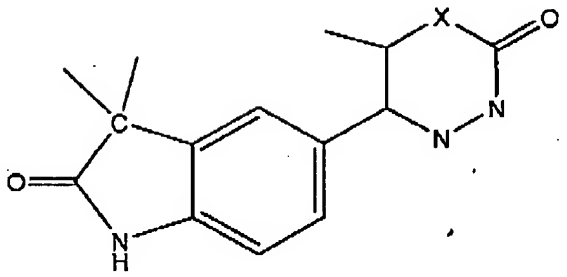

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- The Examiner does not explain how Patani's discosure of certain PDE III modulators in Figure 34, and other structurally distinct Cardiotonic agents in Figure 36, would lead any person of skill in the art to reasonably expect that certain fragments of the scaffold could prove useful in the seach for kinase inhibitors, such as inhibitors of VEGF/KDR.